Conclusions: R0 surgery still represent the milestone of treatment for primary desmoids no matter where the tumour is localized. This is particularly important for huge tumours, where an higher incidence of recurrence is expected.

1442 POSTER

Mina53, a Target Gene of C-Myc, is a Favorable Prognostic Marker in Early Stage Lung Cancer

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Background: Mina53, a novel target gene of c-Myc, is overexpressed in various malignancies. Overexpression of Mina53 has been associated with poor prognosis in esophageal cancer, renal cell carcinoma, and neuroblastoma. We previously demonstrated that Mina53 is overexpressed in lung cancer patients from the early clinical stages. In addition, the enforced expression of Mina53 in NIH/3T3 cells, a mouse fibroblast cell line, induces cell transformation, and Mina53 transfected NIH/3T3 clones produce tumours in nude mice. In this study, we examined the association between disease prognosis and Mina53 expression in lung cancer patients.
Materials and Methods: Mina53 expression was determined by immunohistochemistry and western blotting using lung cancer cell lines and lung cancer tissues. The survival rate was calculated according to the Kaplan–Meier method and the logrank test was used for assessing differences. Biological effects of Mina53 were evaluated by cell proliferation assay, cell cycle analysis, apoptosis assay, and *in vitro* cell invasion assay using Mina53 transfected A549 and H226B cells.
Results: Patients with negative staining for Mina53 had significantly shorter survival than patients with positive staining for Mina53, especially in stage I or with squamous cell carcinoma. We hypothesized that Mina53 exerts different effects according to cancer cell type, inhibiting tumour progression in lung cancer cells. Growth of A549 transfected with pCAGGS/*mina53* (expression plasmid) was inhibited. After transfection of pCAGGS/*mina53* into A549, pre-G0/G1 phase cells increased in a time-dependent manner. In addition, early apoptotic cells were more frequently observed among cells transfected with pCAGGS/*mina53* than those with pCAGGS. Because cell growth inhibition associated with apoptosis was not observed in H226B, we examined the possibility of an effect of Mina53 on cancer cell invasion. The number of invading cells transfected with pCAGGS/*mina53* significantly decreased compared with those with pCAGGS, whereas transfection with *mina53* shRNA increased the number of invading cells.
Conclusions: Mina53 could be a possible favorable prognostic marker, especially in squamous cell carcinoma. Considering the results of biological effects of Mina53, is may play a role on inhibition of cancer progression.

1443 POSTER

High Blood Neutrophil-to-lymphocyte Ratio as an Indicator of Poor Prognosis in Advanced Non Small Cell Lung Cancer

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Background: The neutrophil-to-lymphocyte ratio (NLR) is an index of inflammatory status and in malignant tumours an elevated NLR has been considered as a negative prognostic factor. The aim of this study is to evaluate the clinical significance of the NLR in patients with advanced non-small cell lung cancer (NSCLC) treated with chemotherapy.
Methods: One hundred and seventy one stage IV NSCLC patients diagnosed in our institution between April 2004 and March 2009 were retrospectively reviewed. NRL $\geqslant$5 was considered elevated. Baseline factors analyzed were histology, gender and NLR. Overall survival (OS) and progression-free survival (PFS) were calculated by the Kaplan–Meier method.
Results: Baseline patients characteristics: median age 63 (30−82 years), males 83.6%; adenocarcinoma 40%, large cell carcinoma 21.1%, squamous carcinoma 18.1% and undifferentiated carcinoma 3.5%. All patients were treated with chemotherapy and 36.3% had partial response. NLR was elevated in 60 (35.1%) patients and no differences were detected according clinical characteristics (histology, sex or tumour size). After a median follow-up of 9.1 months, 164 patients relapsed and 159 patients had died. PFS and OS in patients with normal and elevated NLR were 5.6 vs 3.2 months ($p = 0.09$) and 9.1 vs 5.6 months ($p = 0.032$) respectively. Thirty five (60.3%) patients with an elevated basal NLR, normalized the ratio after two cycles of chemotherapy. The OS in patients with persistently abnormal NLR after chemotherapy was of 3.9 vs 8.8 months in patients with normalized NLR ($p = 0.042$). In the multivariate analysis histology (undifferentiated carcinoma) and elevated NLR were independent predictors of survival ($p < 0.01$).
Conclusion: In our analysis, elevated NLR is correlated with worse survival in advanced non-small cell lung cancer These results have highlighted NLR as a potentially useful prognostic marker due to easy accessibility and reproducibility.

1444 POSTER

Evaluation of Hand–foot Syndrome (HFS) as a Potential Biomarker of Sunitinib (SU) Efficacy in Patients (pts) With Metastatic Renal Cell Carcinoma (mRCC) and Gastrointestinal Stromal Tumour (GIST)

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Background: Common side effects of tyrosine kinase inhibitors (TKIs) such as SU include HFS and related skin toxicities. SU is a multitargeted inhibitor of VEGFR, PDGFR and KIT, and is standard of care for the treatment of advanced RCC and imatinib-resistant/intolerant GIST. In this retrospective analysis, correlations between SU-associated HFS and efficacy endpoints were investigated in mRCC and GIST pts from 5 and 4 completed clinical trials, respectively (NCT00054886, NCT00077974, NCT00137423, NCT00083889, NCT00338884, NCT00075218, NCT00137449, NCT00372567; RTKC-0511–013).
Methods: Analyses included data from 1,186 pts with mRCC (n = 770) or GIST (n = 416) who received single-agent SU at 25, 50, or 75 mg/d on an intermittent schedule (4 weeks [wk] on/2 wk off, 2 wk on/2 wk off, or 2 wk on/1 wk off: n = 869; 73%) or at 37.5 mg continuous daily dosing (n = 317; 27%). Median progression-free survival (PFS) and overall survival (OS) were estimated by Kaplan–Meier methods and compared between pts with vs. without HFS by log-rank test. ORR was compared by Pearson's chi-square test. Tumour response was assessed by investigators and adverse events were recorded regularly. Multivariate, time-dependent covariate, and landmark analyses were performed.
Results: Of 1,186 pts, 260 (22%) developed any-grade HFS, compared with 926 (78%) who did not. Pts with mRCC who developed HFS had significantly better ORR (66.5% vs. 31.8%), PFS (14.3 vs. 8.3 mo), and OS (38.3 vs. 18.9 mo) than pts who did not ($P < 0.0001$). Pts with GIST who developed HFS also had significantly better ORR (22.2% vs. 10.7%), PFS (11.0 vs. 5.5 mo), and OS (35.7 vs. 16.6 mo) than pts who did not ($P < 0.01$). SU-associated HFS remained a significant predictor of both PFS and OS in a multivariate analysis (and of OS by time-dependent covariate analysis) in both mRCC and GIST pts. In 6- and 12-wk landmark analyses, pts with mRCC but not GIST who developed HFS had significantly longer OS, with a trend toward longer PFS, than pts who did not.
Conclusions: SU-associated HFS was associated with improved PFS and OS in both mRCC and GIST pts, although the landmark analysis suggests that HFS may not be a reliable biomarker of SU efficacy at early time points.

1445 POSTER

HOXB9, a Gene Promoting Tumour Angiogenesis and Proliferation, is a Novel Prognostic Biomarker in Human Breast Cancer

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Background: Recently, it was reported that HOXB9, a member of homeobox genes, expression promoted tumour neovascularization and metastasis in vitro and in vivo assay. These findings imply that overexpression of HOXB9 contributes to tumour progression through activation of signaling pathways that alter both tumour-specific cell fates and tumour-stromal microenvironment, leading to increased invasion and metastasis. (Hayashida et al., PNAS 2010) In this study, we evaluated the correlation between HOXB9 expression, clinical outcomes, and the clinicopathological variables in breast cancer patients, and the contribution of HOXB9 expression to tumour cell proliferation and angiogenesis.
Materials and Methods: A consecutive series of 141 patients with invasive ductal carcinoma who underwent surgical treatment from January 2004 to January 2005 were examined. HOXB9 protein expression was analyzed immunohistochemically using the anti-human HOXB9 polyclonal antibody. Immunostaining of Ki-67, CD31, and CD34 were also performed to evaluate the association between tumour proliferation, and angiogenesis and HOXB9 expression.
Results: Of 141 tumour specimens immunostained for HOXB9, 69 specimens (48.9%) were positive staining. Statistical analysis revealed

ER and PgR negativity, HER2 positivity, high nuclear grade, lymph node metastasis and large pathological tumour size as significant variables associated with HOXB9 expression. Notably, 12 (92.3%) out of 13 triple negative breast cancer showed HOXB9 expression. The disease-free survival (DFS) and the overall survival were significantly different between the HOXB9 positive and negative group (HR = 20.714, p = 0.001, HR 9.206, p = 0.003, respectively). A Multivariate analysis indicated that HOXB9 expression was the independent prognostic factor for DFS (HR = 15.532, p = 0.009). In subgroup analysis, HOXB9 positive breast tumours showed a significant increase in the number of micro vessel density and the Ki-67 ratio in comparison with HOXB9 negative.
Conclusions: Our results suggest that HOXB9 expression promoting the tumour proliferation and angiogenesis in tumour microenvironment is a significant prognostic biomarker for clinical outcomes in breast cancer patients.

1446 POSTER

Evaluation of CTL Antigen 4 (CTLA-4) Expression as Prognostic Factor in Non-small Cell Lung Cancer (NSCLC)

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Background: CTLA-4, a close homologue to CD28, is a vital negative regulator of T-cell activation and proliferation. Preclinical studies and clinical trials have demonstrated that the administration of antibodies that block CTLA-4 can provoke the elimination or reduction of established tumours. We previously reported that CTLA-4 is expressed by NSCLC cell lines providing evidence of its involvement in apoptosis induction upon engagement with soluble CTLA-4 ligands (Contardi E, Int J Cancer 2005). The present study examined the expression of CTLA-4 on tumour tissues of patients (pts) with radically resected stage I-IIIA NSCLC.
Materials and Methods: Tumour tissue samples from 82 pts who underwent surgery between 7/2005−3/2007 were analyzed for expression of CTLA-4 using immunohistochemistry (IHC). Viable tumour was sampled in triplicate for tissue microarray analysis, and slides were stained by IHC with 14D3 mAb (eBioscence, San Diego, CA, USA). All tissue arrays were independently scored by two observers (M.T. and S.S.), blinded to the patients. CTLA-4 score was calculated using the following formula: $(1+I)\times PC$, where I is the staining intensity and PC the percentage of tumour cells that stained at each intensity, respectively. The score median value was a priori chosen as the cutoff point for classifying tumours as CTLA-4-negative (score $\leqslant$20) and positive (>20). Results: The median follow-up time was 41 months (range 28−54), and 27 deaths were observed. CTLA-4 expression was positive in 48% of tumours and similar in males and females (47 vs 47%), age $\leqslant$70 and >70 (46 vs 49%), ex-never smokers and current smokers (46 vs 47%), whereas was higher in non-squamous than in squamous carcinoma (53 vs 36%). Cox's multiple regression analysis identified stage and CTLA-4 expression as the only variables associated with survival. The hazard ratio (HR) was 2.76, (95% CI, 0.9−8.3; p = 0.07) and 6.61 (95% CI, 2.6–16.8; $p \leqslant 0.001$) for tumour stage II and III compared to stage I respectively, and 0.39 (95% CI, 0.2−0.9; p = 0.03) for CTLA-4 score >20. Conclusions: Our results demonstrate an association between CTLA-4 expression and increased overall survival in NSCLC pts suggesting a prognostic role for CTLA-4 in NSCLC. An increased CTLA-4 expression may contribute to NSCLC progression by modulating the interaction of microscopic disease with CTLA-4 ligand-expressing cells leading to NSCLC cell death.

1447 POSTER

First-line Treatment of Non-Small Cell Lung Cancer Under Routine Conditions: Observational Study (FRAME)

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Background: FRAME is a non-interventional, prospective observational study of first-line treatment (FLT) of advanced non-small cell lung cancer (NSCLC) in routine disease management. This analysis of baseline data provides insights to what extent histological sub-typing and the use of additional prognostic or predictive biomarkers are currently considered for differential therapeutic decisions.
Material and Methods: 1569 patients diagnosed with stage IIIB/IV NSCLC who initiated FLT with any platinum-based doublet chemotherapy, with or without targeted agents, were observed in routine practice. Patients' baseline characteristics, first-line treatment and all diagnostic procedures were collected upon study enrolment.
Results: FRAME was performed in 11 EU countries; baseline characteristics reflect this geographic location with a predominance of Caucasian patients (1.3% Asian origin) and smokers (84%). Median age was 64 yrs (33−87), females: 29%, stage IV: 77%, performance status 0−1: 82%.
Histological diagnosis was obtained in 80% while only cytological was obtained in 20% of patients. Not Otherwise Specified (NOS) was final diagnosis for 11% of patients. Most common reasons for NOS diagnosis were: 'Sub-typing technically not possible' (43%) and 'Not important for treatment decision' (40%).
At least one of the IHC markers was used in 54% of cases (p63−9%, ck14−2%, ck7−39%, ck5/6−18%, TTF-1−48%, cd56−4%, others-24%). EGFR, ERCC1, TS, or other predictive biomarkers were assessed in 21% of pts. EGFR mutation was positive in 12% of 308 tested patients.
FLTs were platinum-based therapy plus one of: pemetrexed 36%, gemcitabine 23%, taxanes 19%, vinorelbine 19%, others 3%. Ninety-seven percent of patients treated with pemetrexed and 97% with bevacizumab had a diagnosis of non-squamous NSCLC. Concurrent targeted agents were administered in 8% of cases (mostly bevacizumab, *7%).* Key factors identified by physicians for choice of FLT were 'Histopathological/cytological diagnosis' 77%, 'Performance status' 63% and 'Age' 53%.
Conclusions: In this large non-interventional study of FLT for NSCLC, a relatively high level of histological testing was observed (80%), likely resulting in low NOS (11%) diagnosis. In addition, IHC (54%) and predictive biomarkers (21%) were routinely assessed.

1448 POSTER

Correlation of Topoisomerase IIα and MIB-1 Expression on Tissue Microarray of Breast Carcinomas

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Background: Breast cancer is the most common malignancy in females. Measurement of cell proliferation in breast carcinomas was shown to have prognostic importance, primarily measured by MIB-1 labelling index. A nucleic enzyme, topoisomerase IIα (TopIIa) expression was reported to be linked to cell proliferation that estimated the number of proliferative cells in actively cycling cells of both normal and neoplastic cells. The aim of this study was to evaluate TopIIa protein expression in breast carcinomas and compare with MIB-1 expression. We also analyzed TopIIa correlation with known outcome variables.
Materials and Methods: Using tissue microarray (TMA), we immunostained 70 breast carcinomas for TopIIa and MIB-1. A TopIIa staining index (TI) was calculated by the mean number of positive cells per high power magnification and was interpreted as positive (TI > 1) and negative (TI < 1) while MIB-1 was considered positive if 10% or more of the nuclei were stained.
Results: Forty-one of 70 breast carcinomas (59%) were TI positive (mean, 15.04 ± 18.09; range, 1.12 to 85.24) and 29 (41%) cases were TI negative (mean, 0.04 ± 0.12; range, 0–0.46). Our data demonstrated 64.7% concordance between TopIIa with MIB-1 expression (kappa = 0.239, p = 0.042). There were no significant association observed in this study between TopIIa overexpression and other known outcomes including lymph node metastases (46%, p = 0.467), low tumour grade (42%, p = 0.353), tumour size greater than 2 cm (71%, p = 0.634), ER positive (78%, p = 0.145), PR positive (76%, p = 0.093) and HER-2 overexpression (22%, p = 0.899).
Conclusions: A significant association between TopIIa and MIB-1 overexpression suggests that TopIIa maybe a potential proliferative marker that is similar or better than MIB-1.